A Method to Estimate Unbiased Partial Time-Frequency Spectra: Application to Repolarization Variability Changes Unrelated to Heart Rate Variability

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MARIE CURIE ACTIONS

Barts Health NHS Trust

UCL

Dynamic interactions

Biological signals:

- Non-stationary
- Coupled to other signals

→ **Dynamic interactions**

- Insight into a specific physiological system
- Clinical applications

Time-frequency analysis

- **TF Spectra**: Amplitude of non-stationary oscillations.

  Orini et al, MBEC 2010
- **TF Coherence**: Strength of linear coupling + similarity.

  Orini et al, TBME 2012; Gil, Orini et al., Physio Meas, 2010
- **TF phase difference**: Degree of synchronization

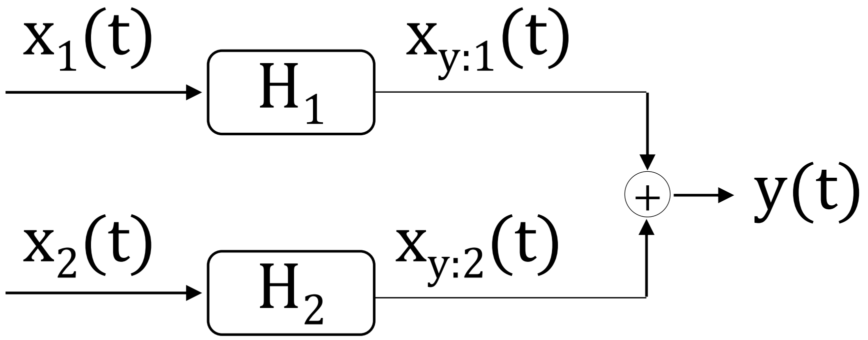
  Orini et al, EMBC 2011
- **TF Indices**: e.g. Baroreflex sensitivity

  Orini et al, Physio Meas 2012
- **TF partial coherence**: Multivariate cardiovascular interactions

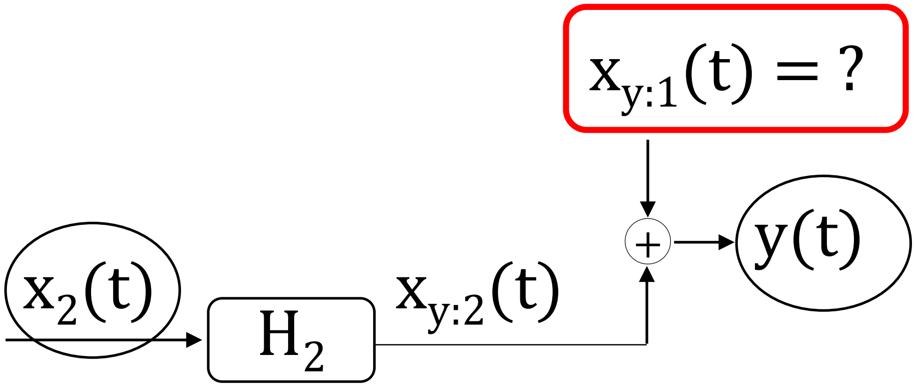
  Orini et al, Eurasip 2012
- **TF partial spectra**: Separate coherent/residual components

  Widjaja, Orini et al, CMMM 2013

Time-Frequency Partial Spectra



Time-Frequency Partial Spectra



$$y(t) = x_{y:1}(t) + x_{y:2}(t)$$

If $x_{y:1}(t)$ and $x_{y:2}(t)$ are uncorrelated:

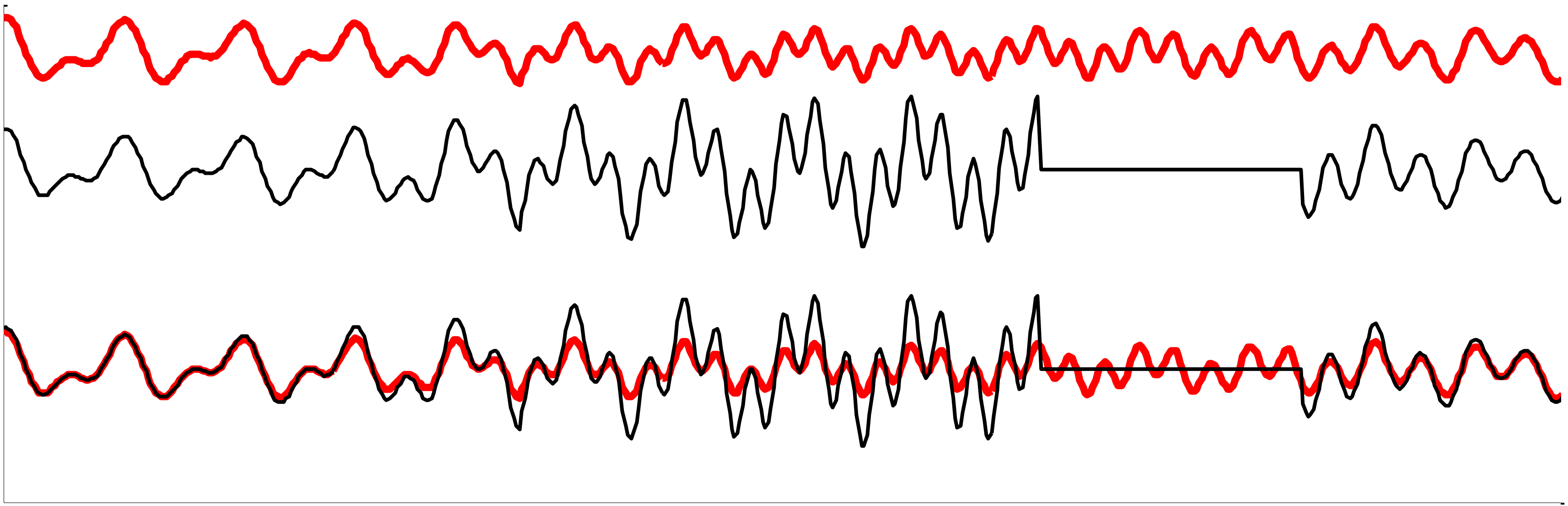
$$S_y(f) = S_{y:1}(f) + S_{y:2}(f) = \boxed{S_y(f) - S_{y:2}(f)} + \boxed{S_{y:2}(f)}$$

Residual Spectrum **Coherent Spectrum**

$$S_{y:1}(f) = S_y(f) - S_{y:2}(f) = (1 - |\gamma_{y,2}(f)|^2)\, S_y(t)$$

$$S_{y:1}(t,f) = S_{y:1}(t,f) - S_{y:2}(t,f) = (1 - \boxed{|\gamma_{y,2}(t,f)|^2})\, S_y(t,f)$$ **TF Extension**

Time-frequency coherence

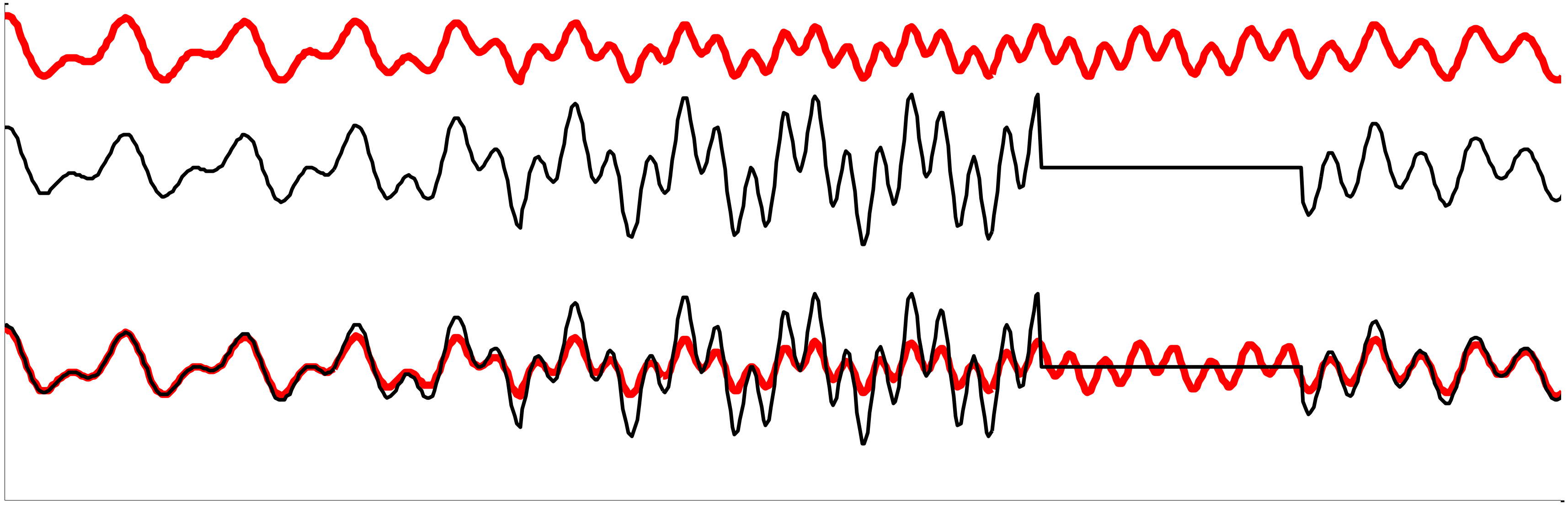


$$\gamma_{xy}(t,f) = \frac{\left|S_{xy}(t,f)\right|}{\sqrt{S_{xx}(t,f) + S_{yy(t,f)}}}$$

$$S_{xy}(t,f) = \iint \phi(t,f) W_{xy}(\tau - t, \nu - f) d\nu d\tau$$ (Cross) Spectrum

$$W(t,f) = \int x(t + {}^{\tau}/_{2}) y^{*}(t - {}^{\tau}/_{2}) e^{-i2\pi f\tau} d\tau$$ Wigner-Ville Distribution

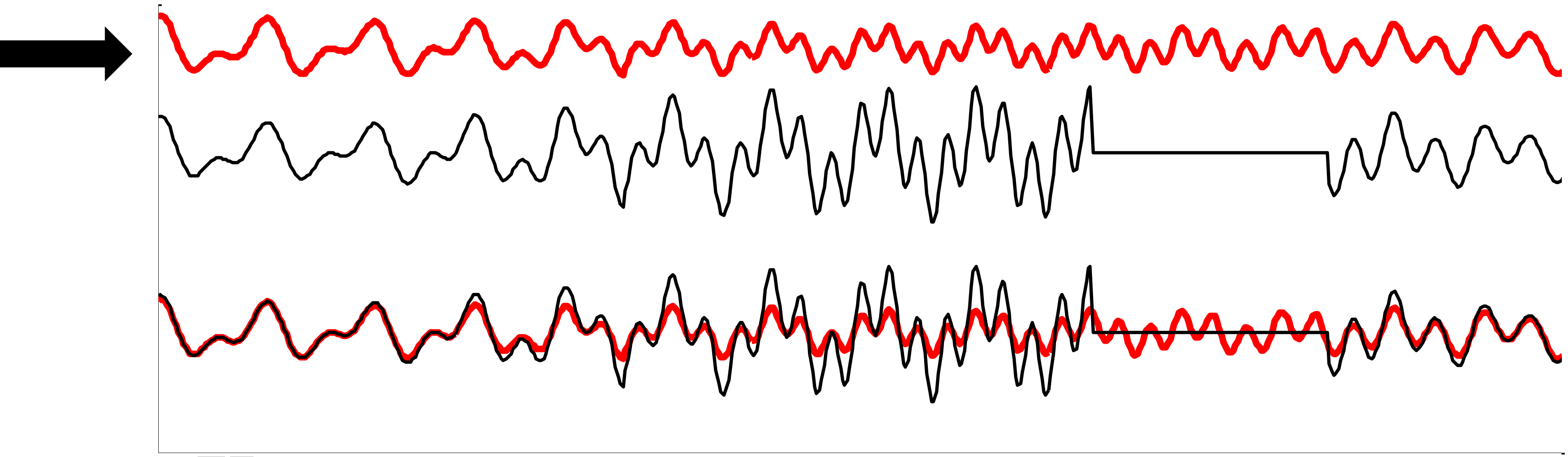
Time-frequency coherence



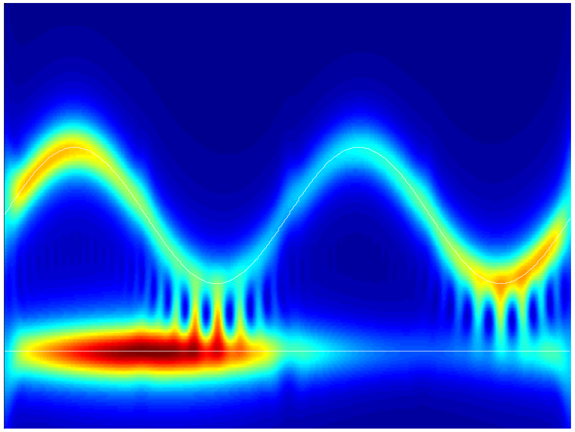
TFC quantifies the **strength of local linear coupling** between 2 non stationary signals

- TFC = 1 → Perfect local linear coupling
- TFC = 0 → Uncoupled

Time-frequency coherence



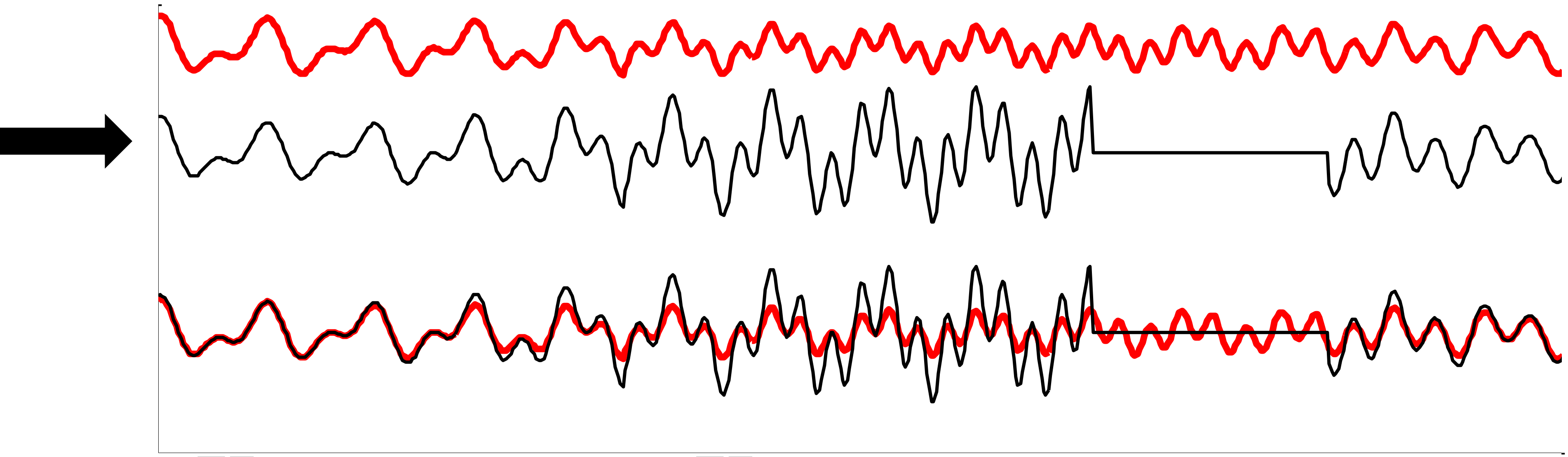
TF spectrum



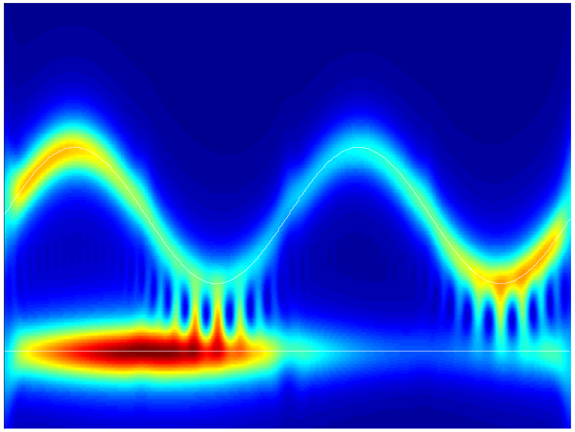
Frequency [Hz]

Time [s]

Time-frequency coherence

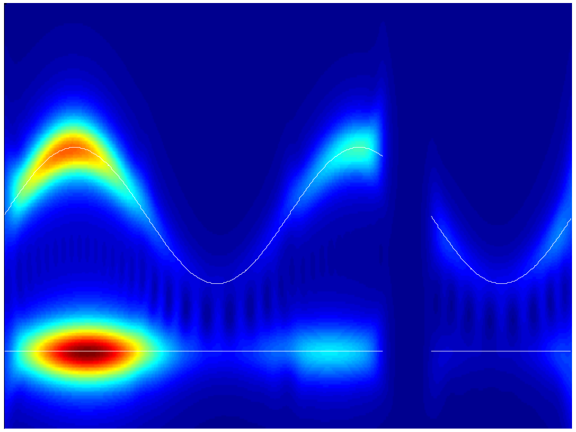


TF spectrum



Time [s]

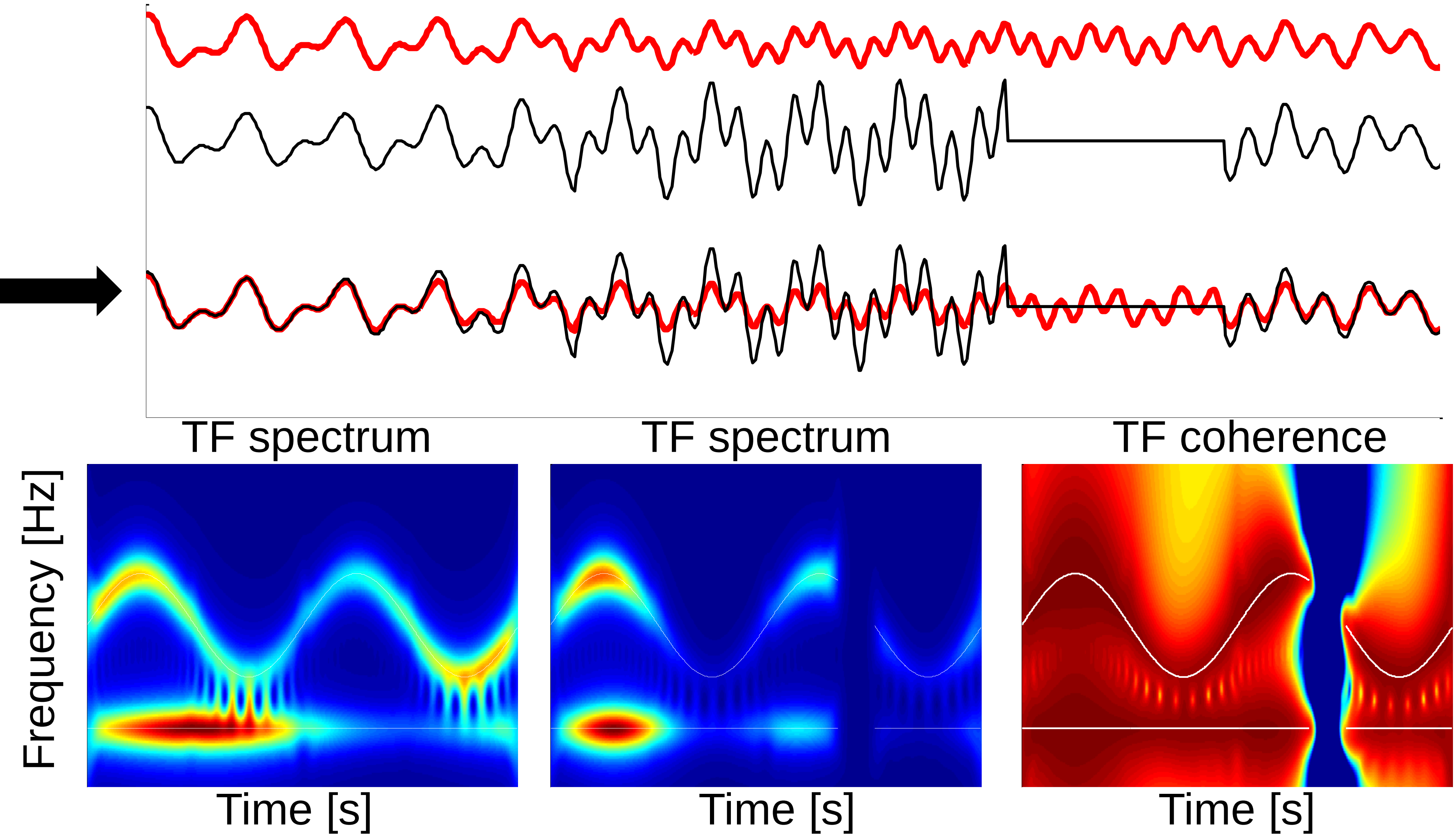
TF spectrum



Time [s]

Frequency [Hz]

Time-frequency coherence

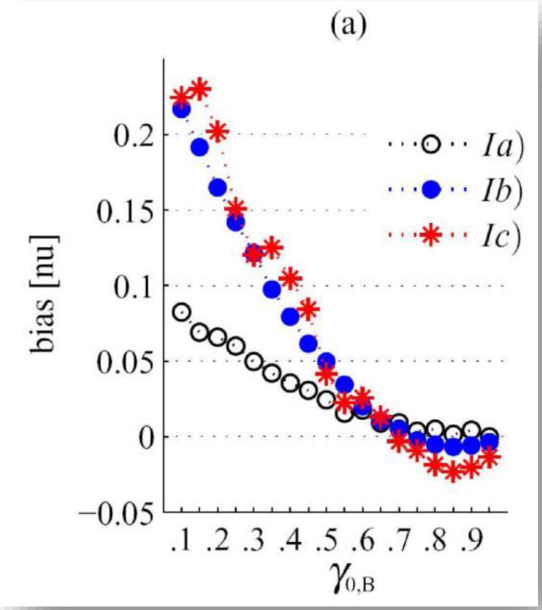


Biased Estimators

- Coherence estimators are biased $(\hat{\gamma} \neq \gamma_0)$
- Bias depends on estimator's parameters

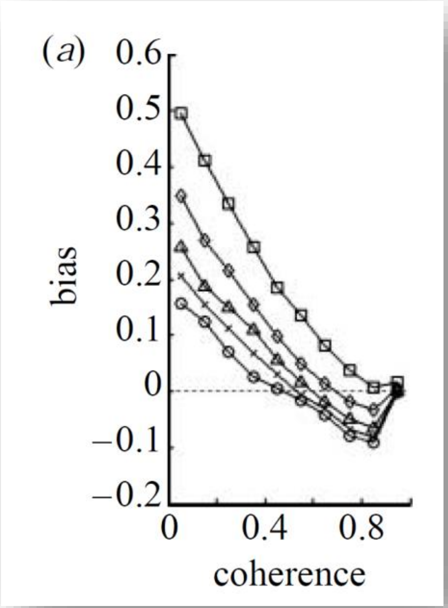
→ Partial Spectra are Biased

Coherence by TFD



Orini et al, CinC 2009

Coherence by CWT



Keissar et al, Phil Trans R Soc A 2009

Biased Estimators

- Coherence estimators are biased $(\hat{\gamma} \neq \gamma_0)$
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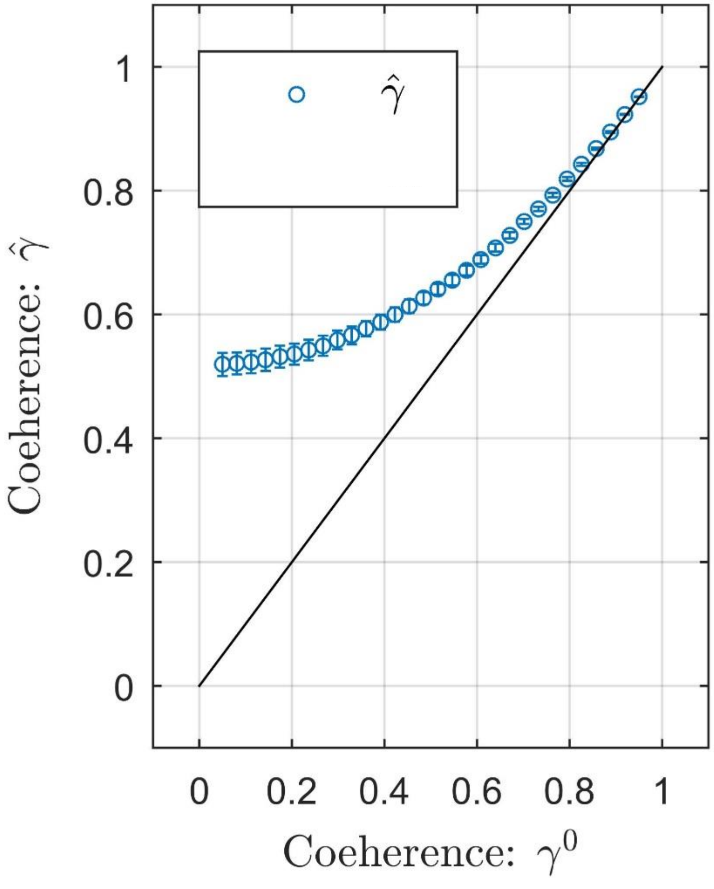
→ Partial Spectra are Biased

Proposed solution

- Assess the bias (theoretical – estimated)
- Estimate a correction function
- Map estimated coherence into unbiased coherence

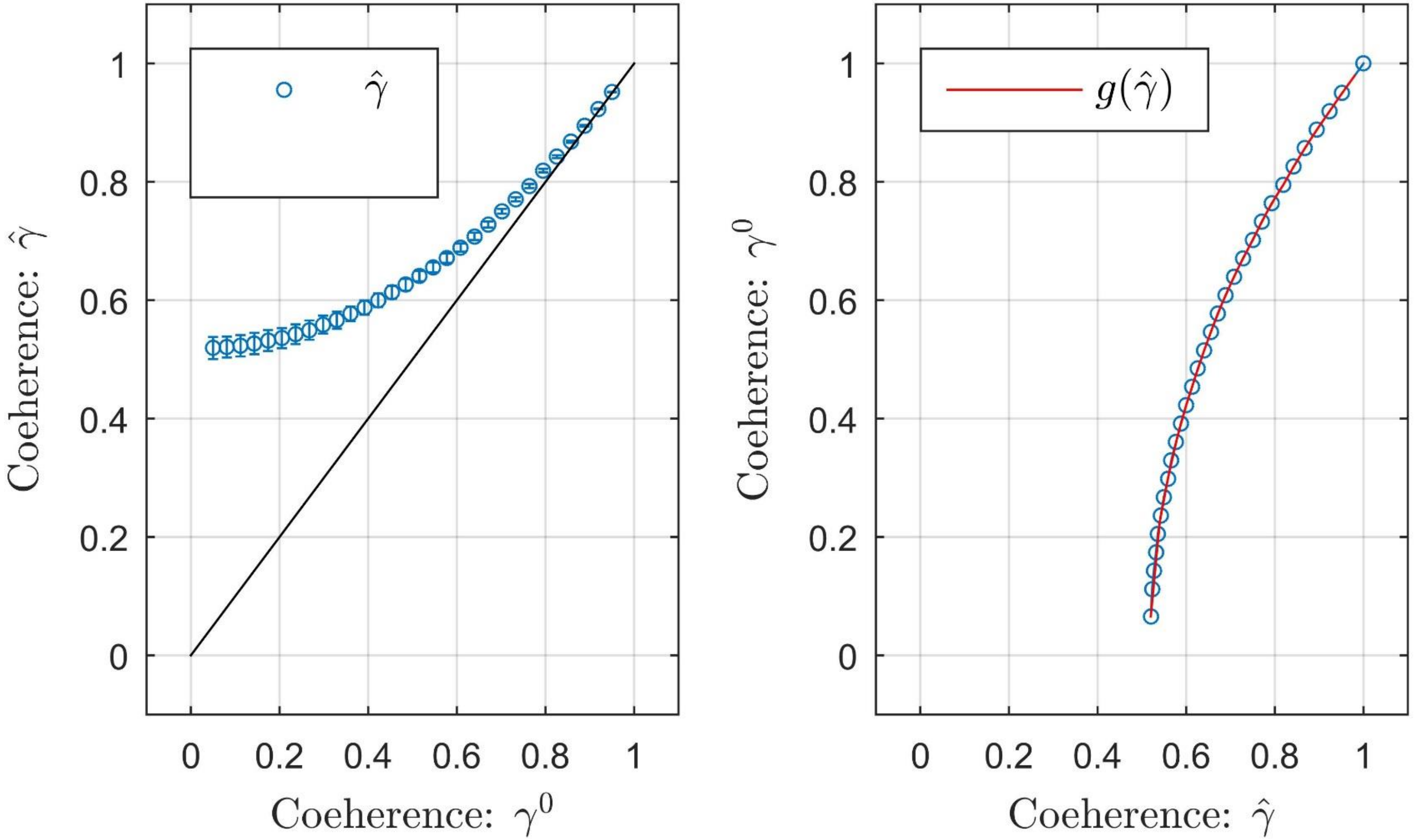
Unbiased Time-Frequency Coherence

$$\hat{\gamma}(t,f) = h\left(\gamma^0(t,f)\right)$$



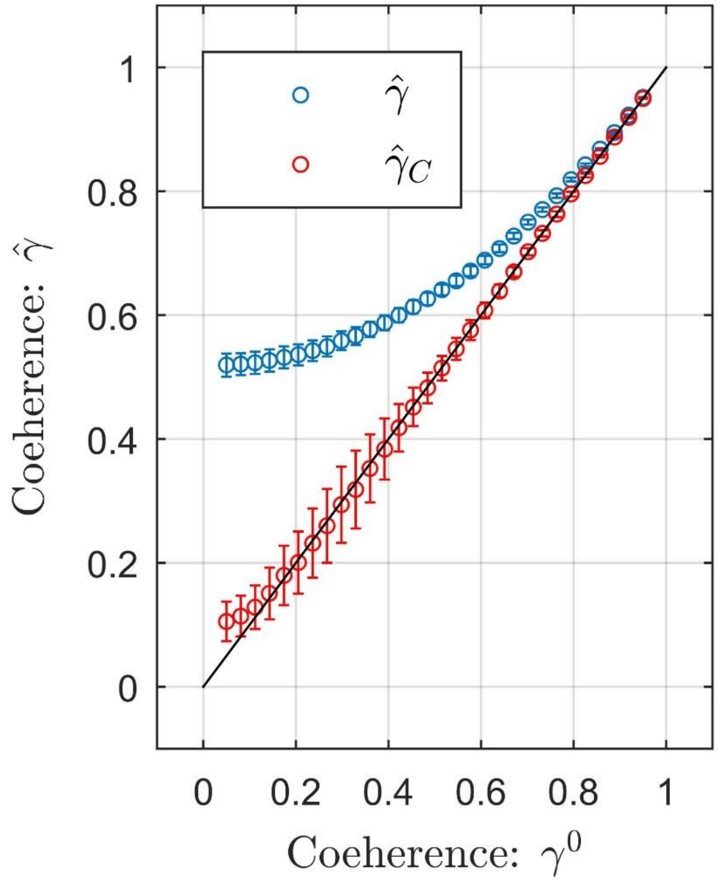
Unbiased Time-Frequency Coherence

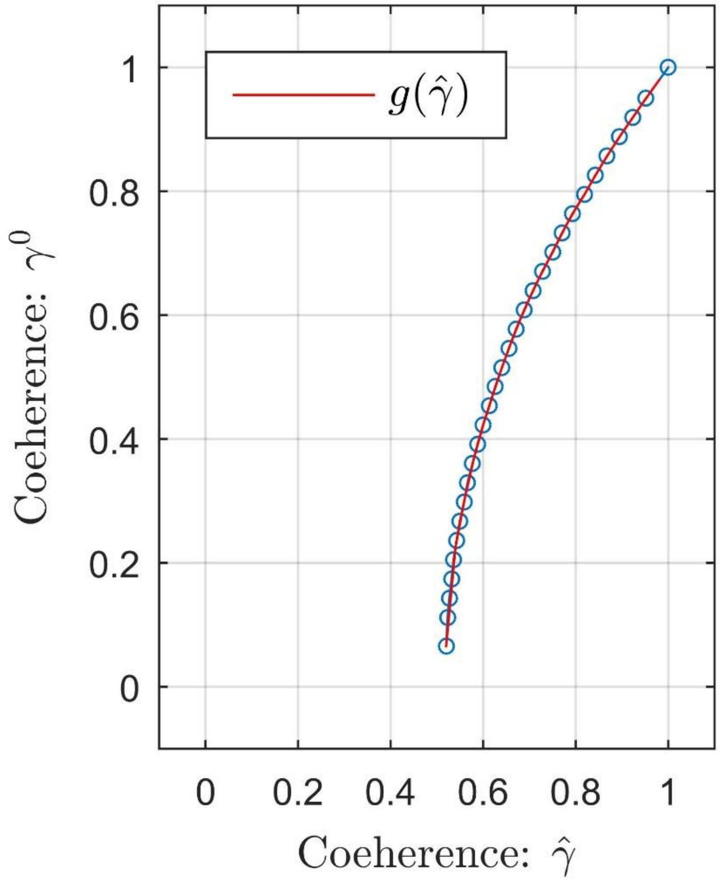
$$\hat{\gamma}(t,f) = h(\gamma^0(t,f)) \Rightarrow \boldsymbol{g}(\cdot) \approx \boldsymbol{h}^{-1}(\cdot)$$



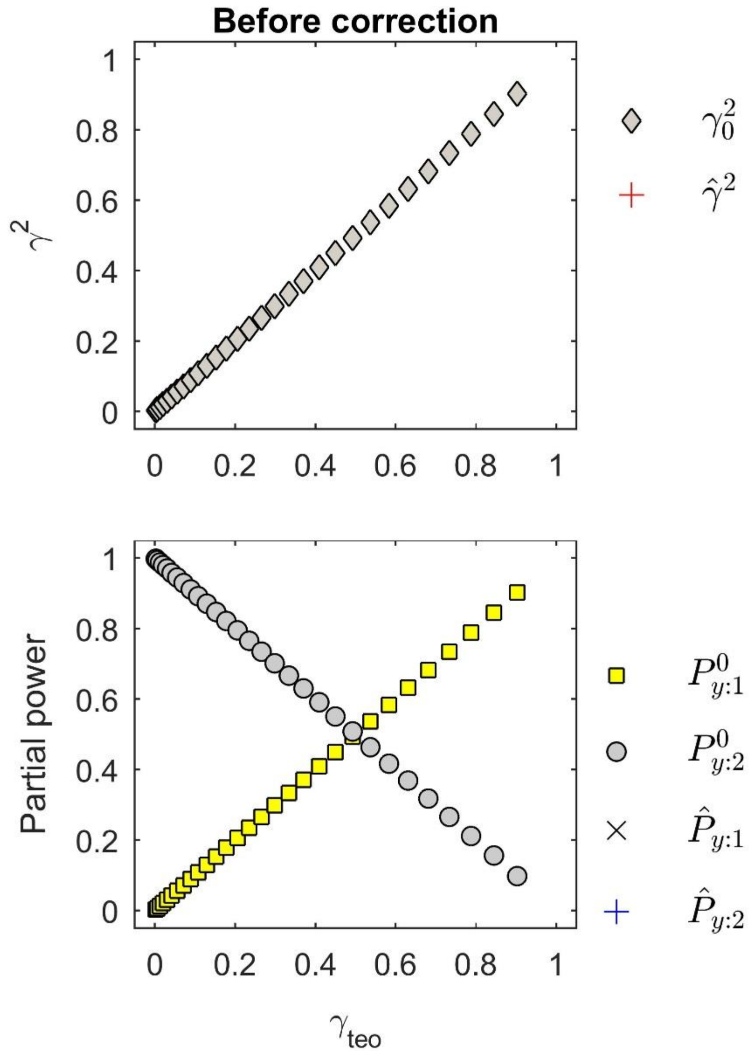
Unbiased Time-Frequency Coherence

$$\hat{\gamma}(t,f) = h(\gamma^0(t,f)) \Rightarrow g(\cdot) \approx h^{-1}(\cdot) \Rightarrow \boldsymbol{\hat{\gamma}_C(t,f) = g\big(\hat{\gamma}(t,f)\big) \approx \gamma^0(t,f)}$$

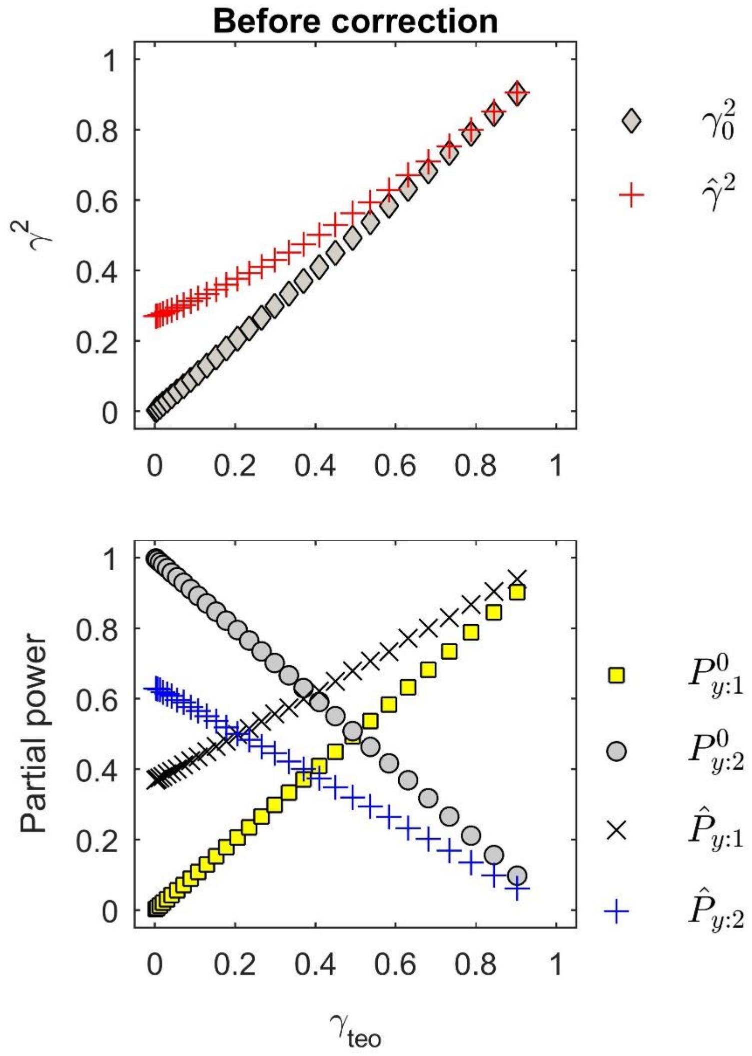




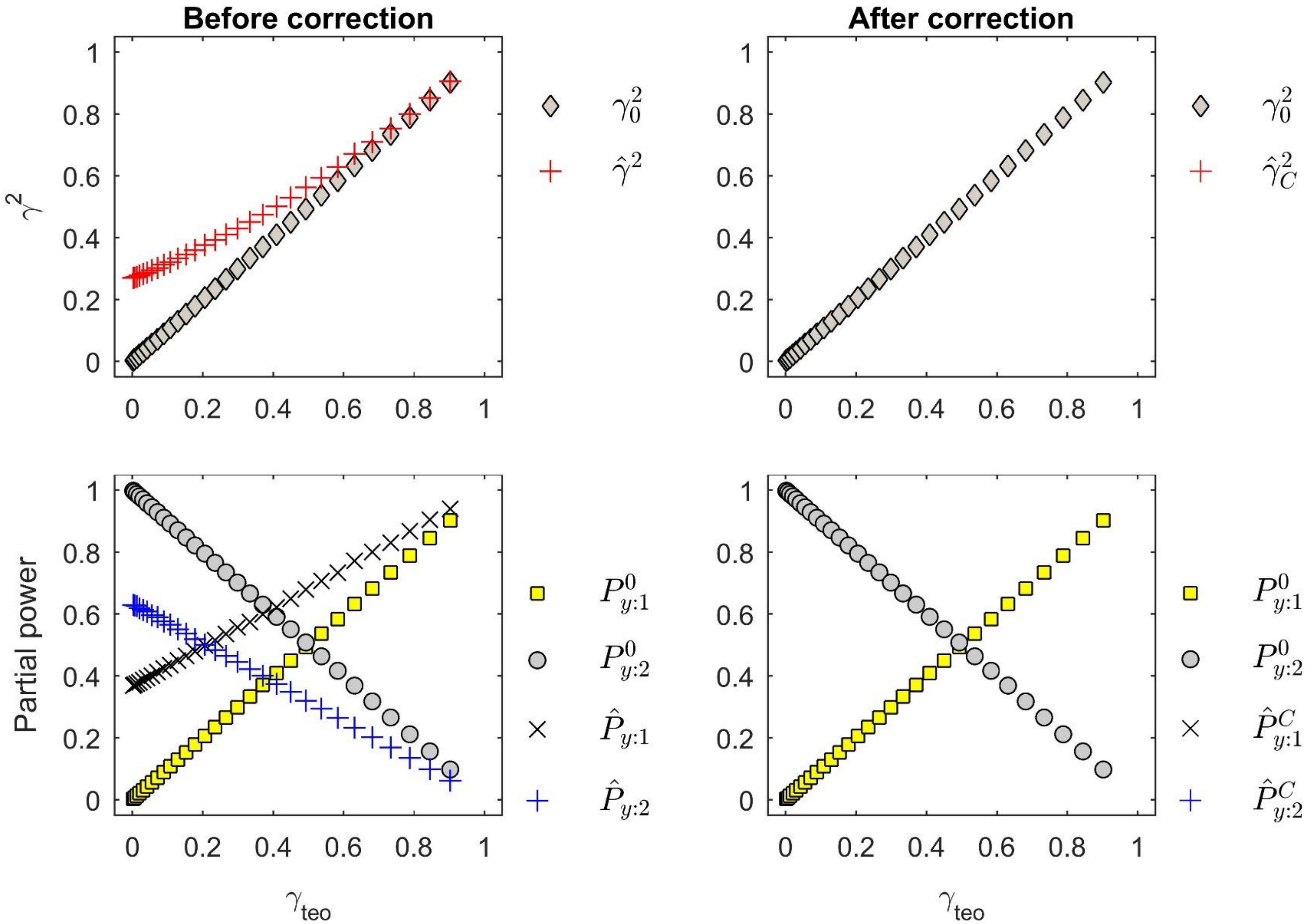
Unbiased Time-Frequency Coherence



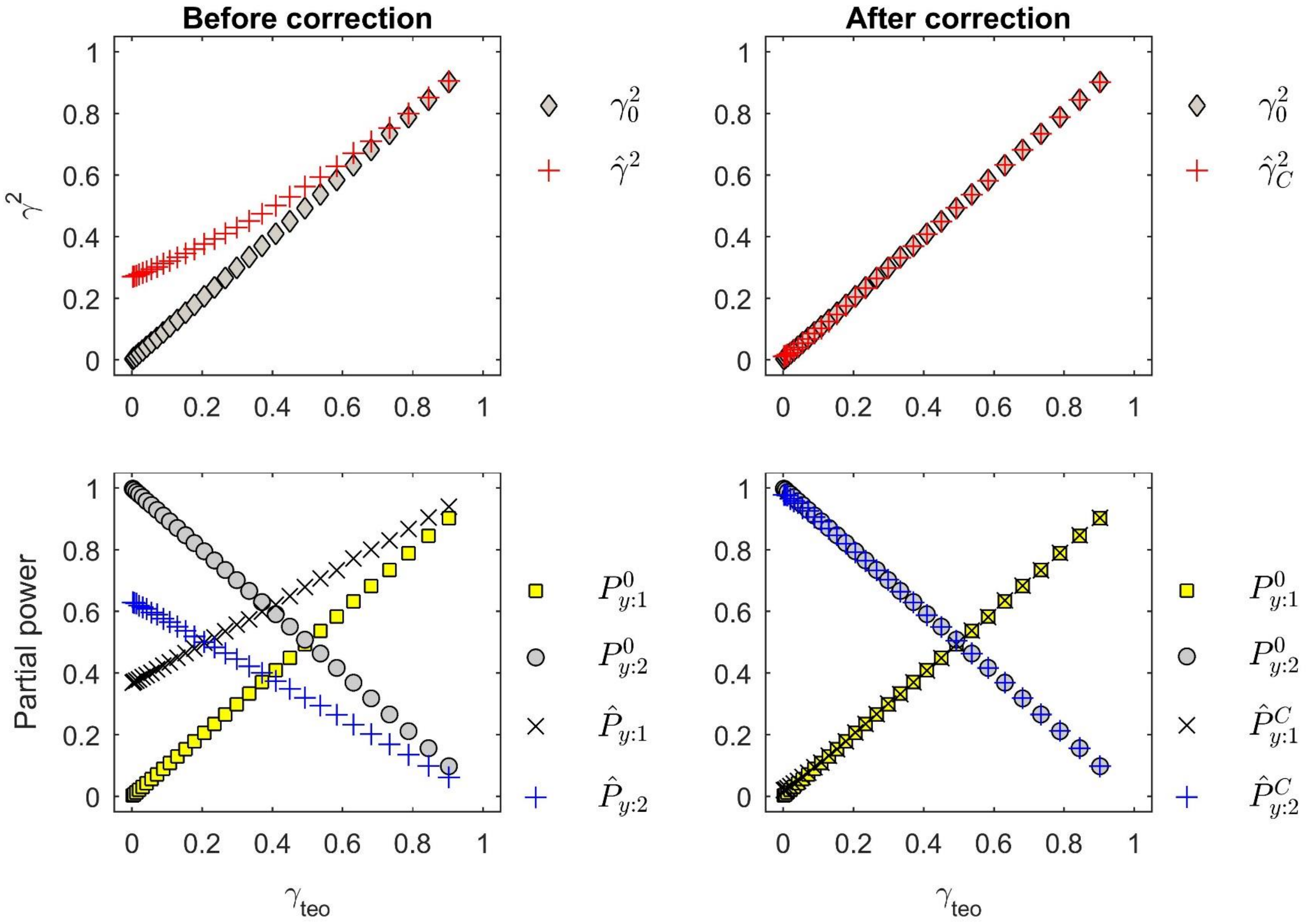
Unbiased Time-Frequency Coherence



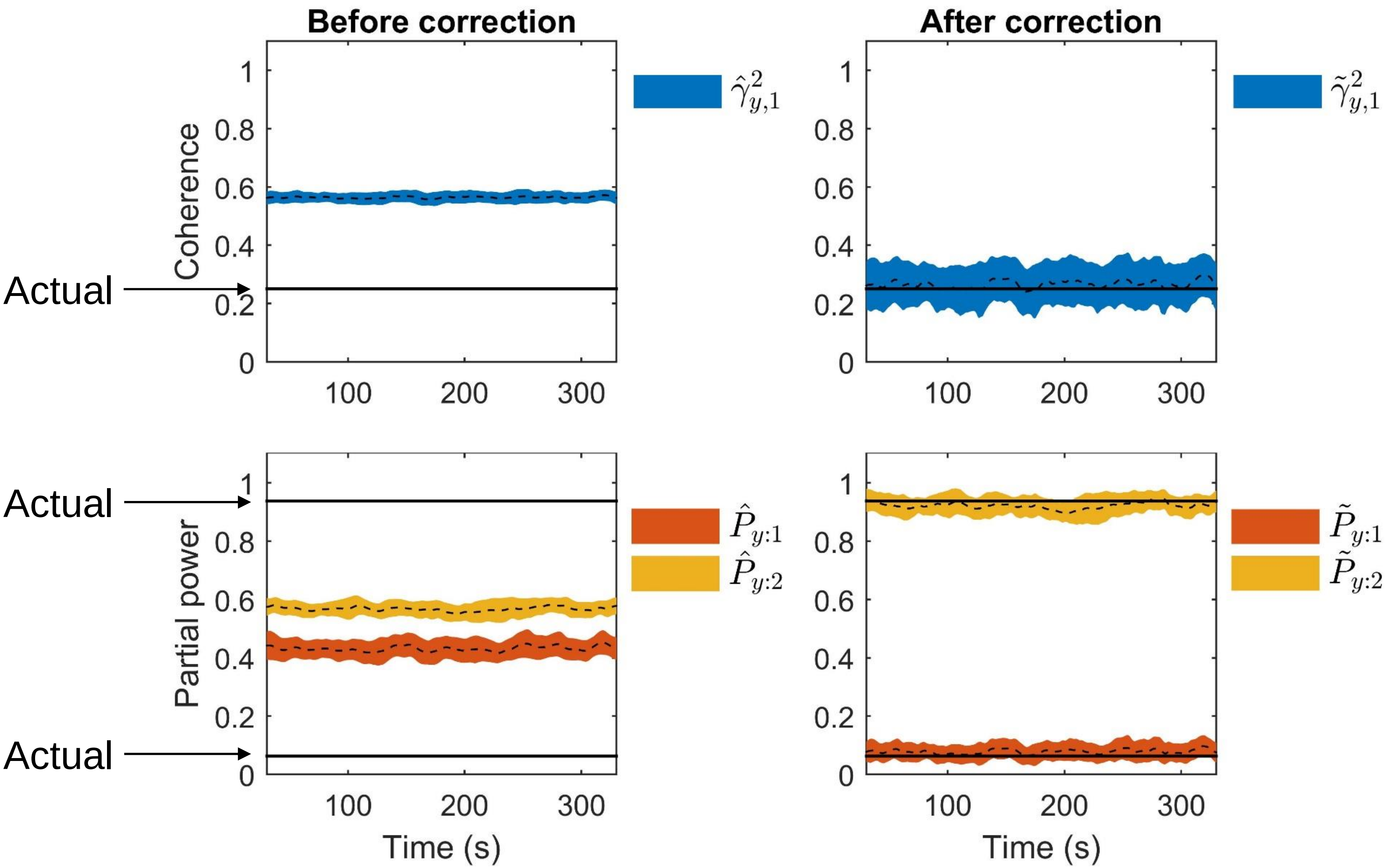
Unbiased Time-Frequency Coherence



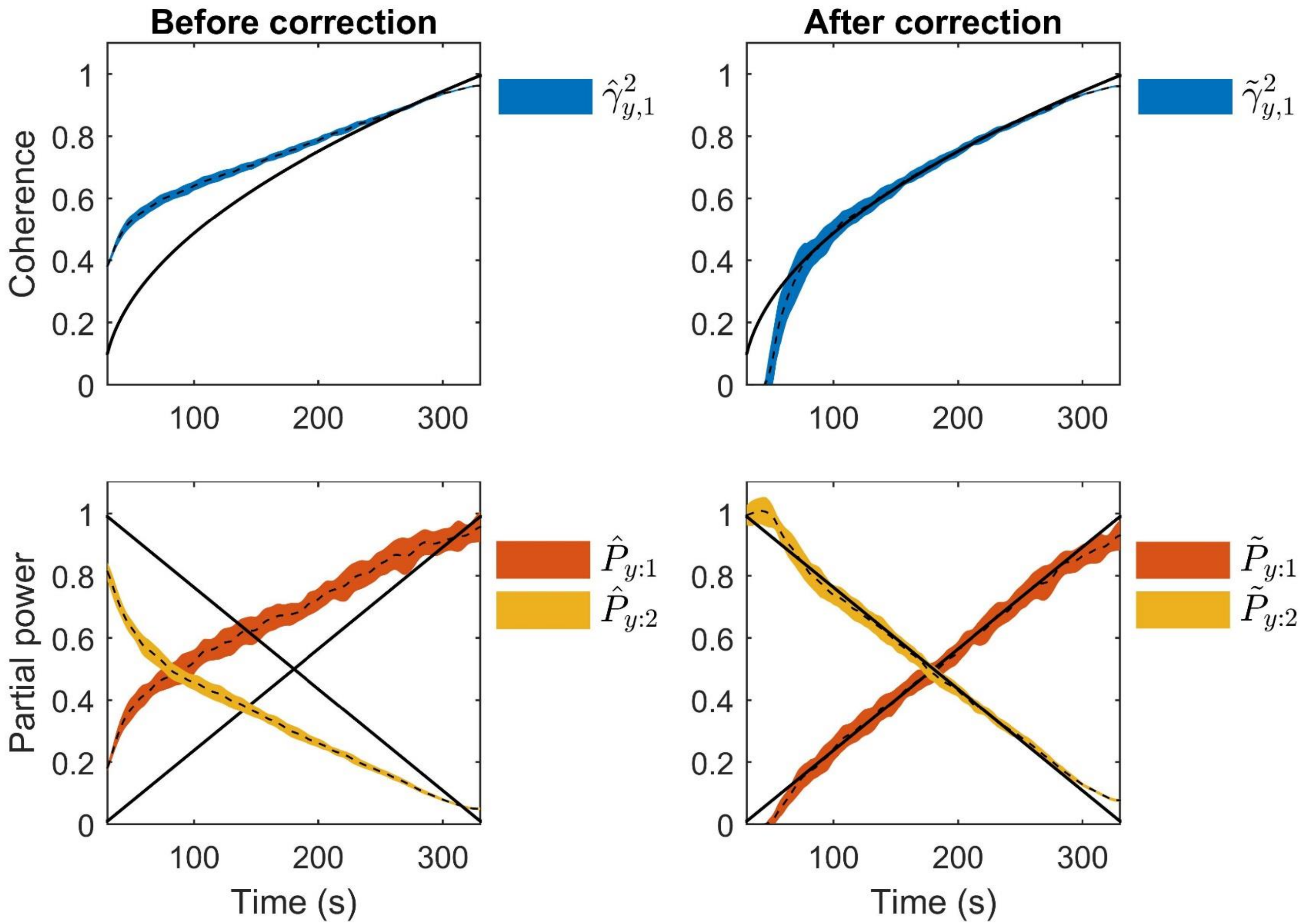
Unbiased Time-Frequency Coherence



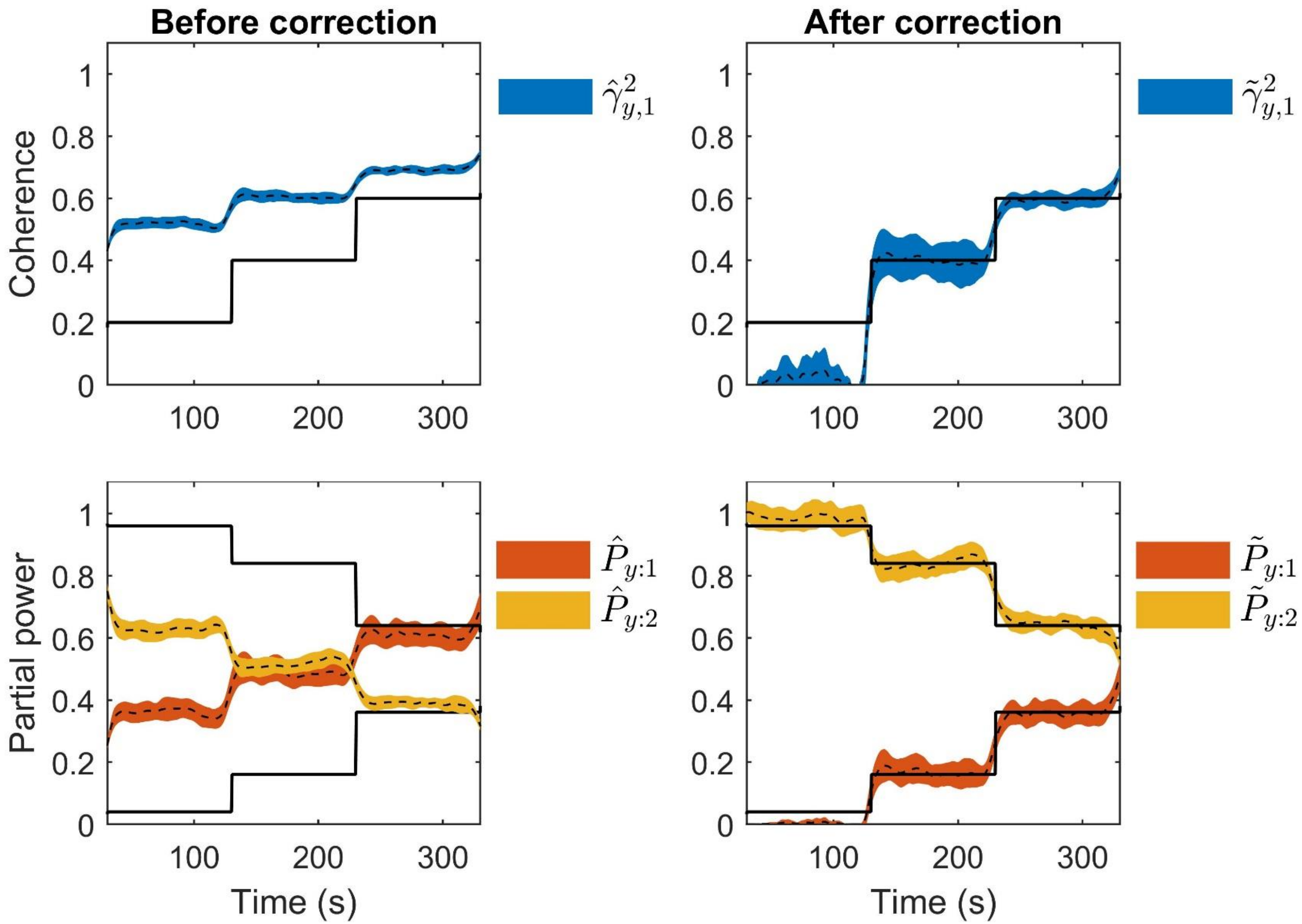
Application : Examples



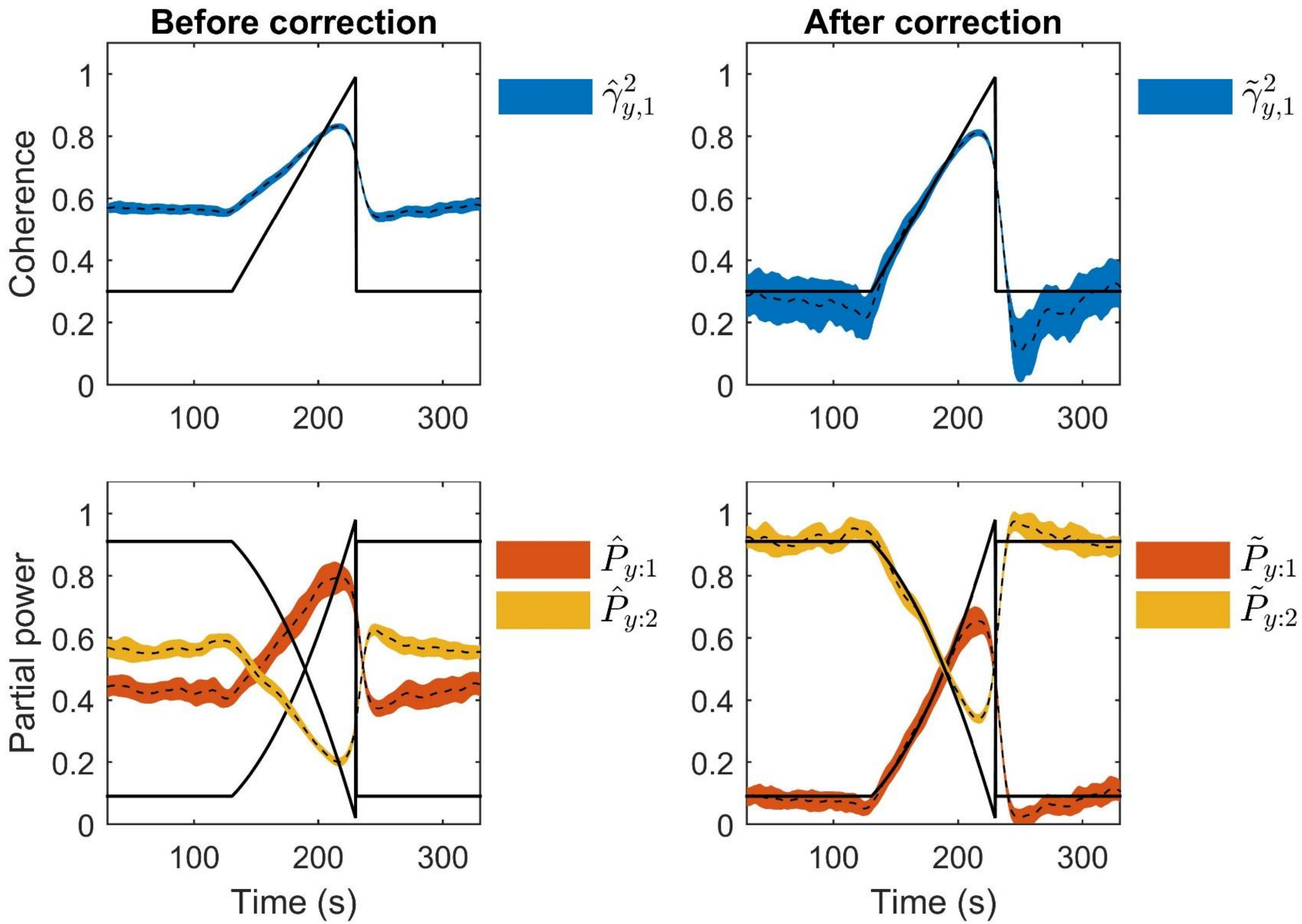
Application : Examples



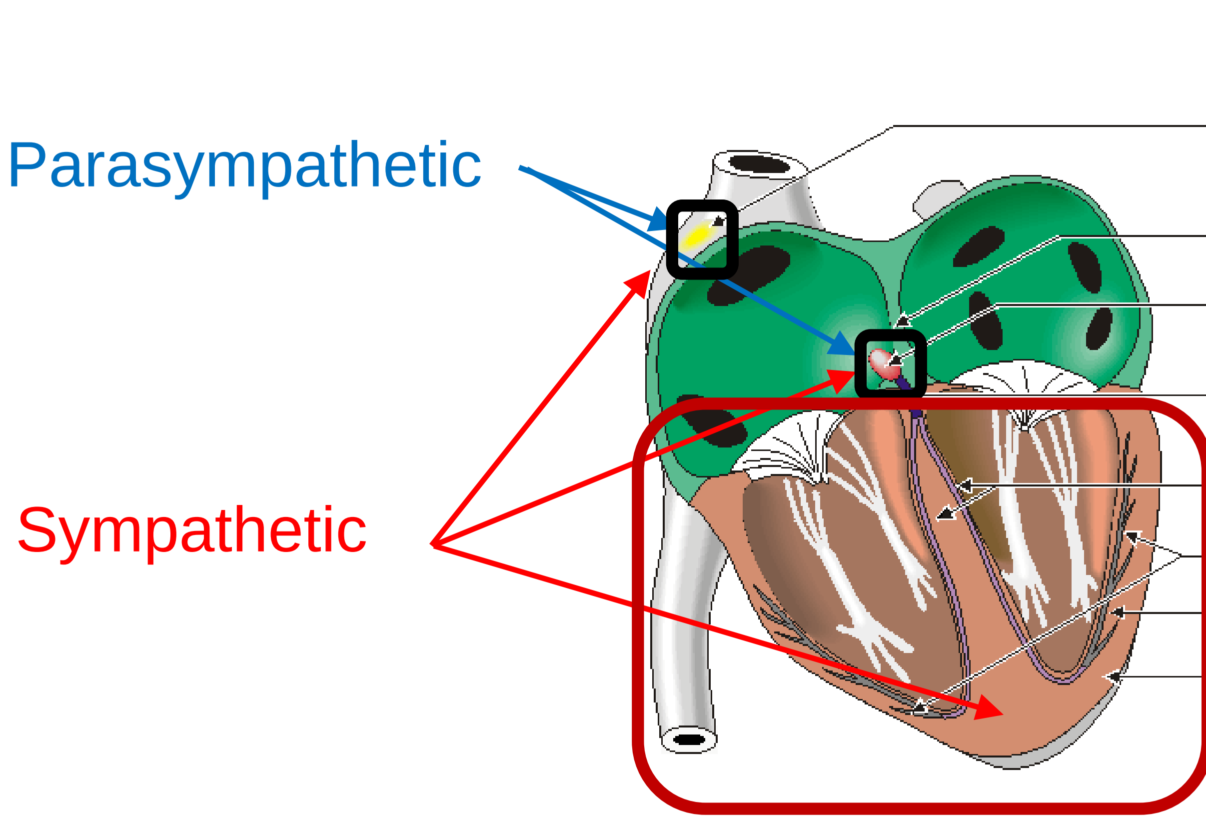
Application : Examples

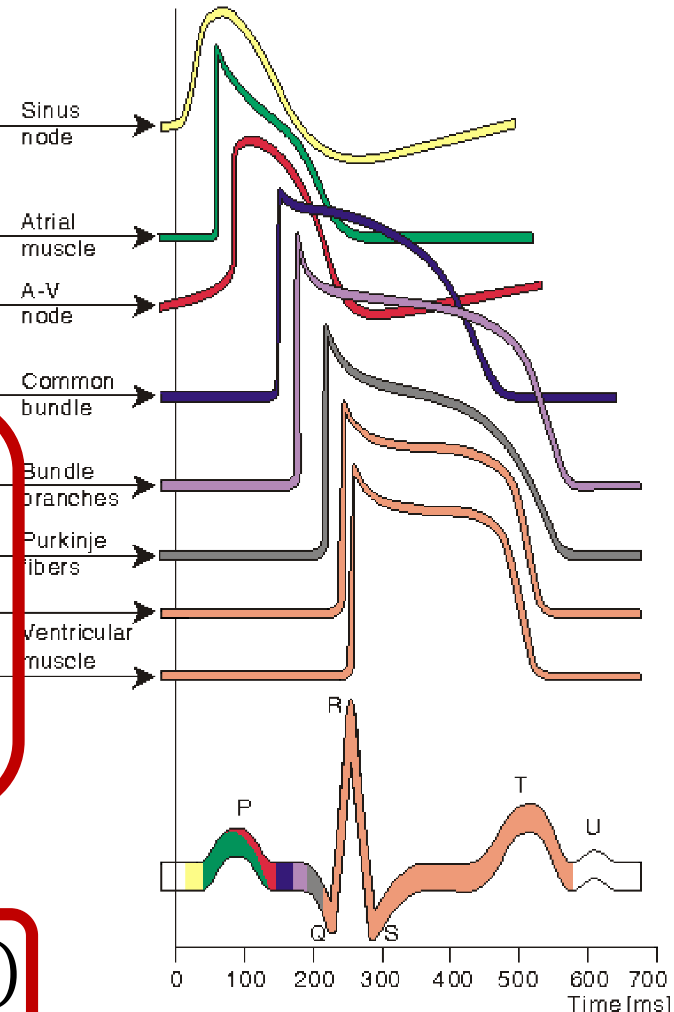


Application : Examples



RRV-Unrelated QT Variability

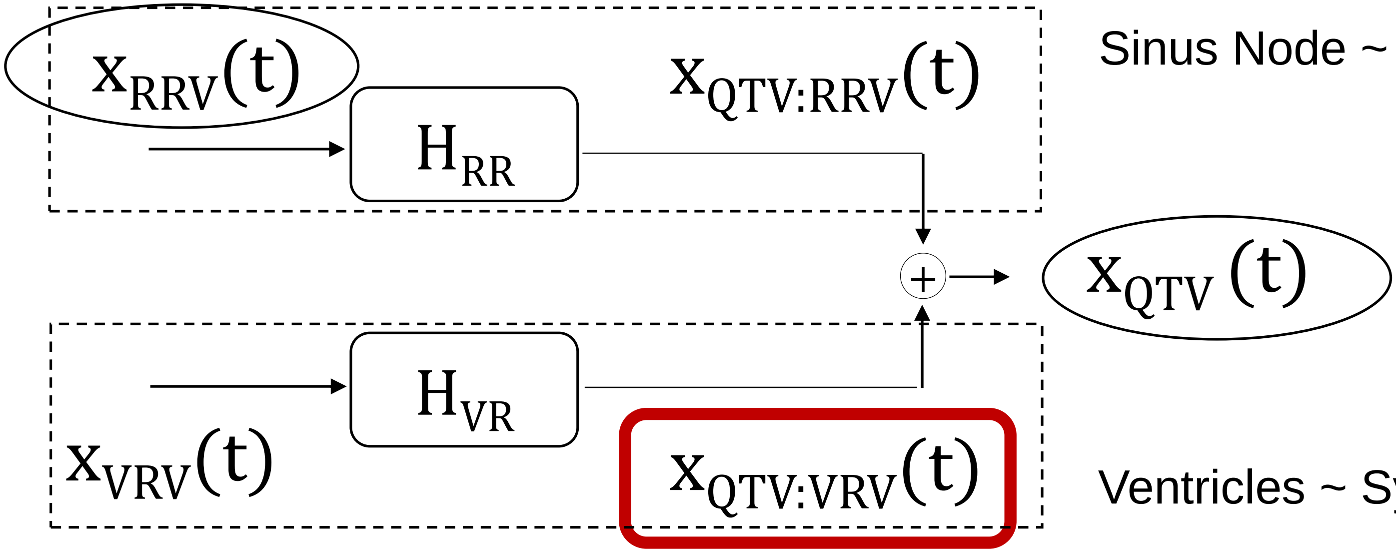




http://www.bem.fi/

$$x_{QTV}(t) = \boxed{x_{QTV:RRV}(t)} + \boxed{x_{QTV:VRV}(t)}$$

RRV-Unrelated QT Variability



Sinus Node ~ Parasympathetic

Ventricles ~ Sympathetic

$$x_{QTV}(t) = x_{QTV:RRV}(t) + x_{QTV:VRV}(t)$$

Short term QT variability

Condition	QTV
Age	↑
Gender	=
Exercise	↑
Cardiac abnormalities (LQTS)	↑
VT/VF, SCD, Cardiovascular mortality	↑**(10) /= (3)**
Cardiomyopathies, CAD, Hypertension	↑
Increased sympathetic activity	↑**(3)**
Disturbed cardiac autonomous regulation	↑ **(6)**
Sympathomimetic drugs	↑
β-blockers	↓

Niemeijer et al. "Short-term QT variability markers…", *Heart,* **2014**

Baumert, M. et al., "QT interval variability in body surface ECG…" Europace, 2016, -

Short term QT variability

Condition	QTV
Disturbed cardiac autonomous regulation	↑ (6)
Sympathomimetic drugs	↑
β-blockers	↓

"QT variability markers are potentially useful determinants of ventricular arrhythmias, (sudden) cardiac death and total mortality, both in the context of risk stratification and drug safety. Also, results suggest that the QTV may be used as a marker of neural regulation of cardiac function."

QT variability unrelated to HRV may be a better predictor and a better marker of sympathetic activation …

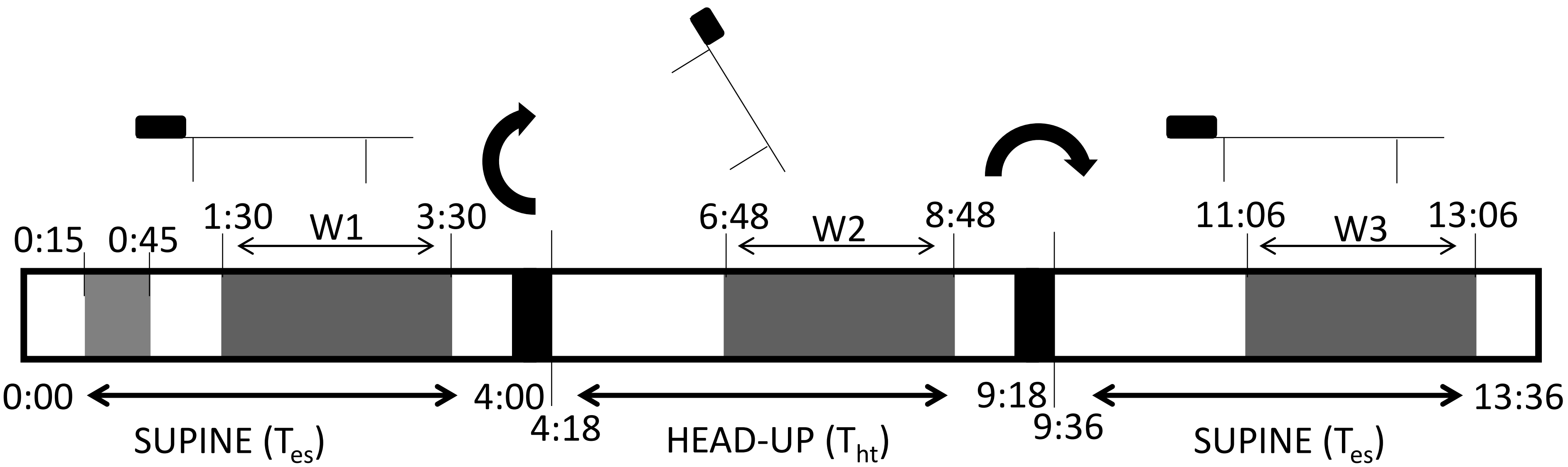
Niemeijer et al. "Short-term QT variability markers…", *Heart,* **2014**

Baumert, M. et al., "QT interval variability in body surface ECG…" Europace, 2016, -

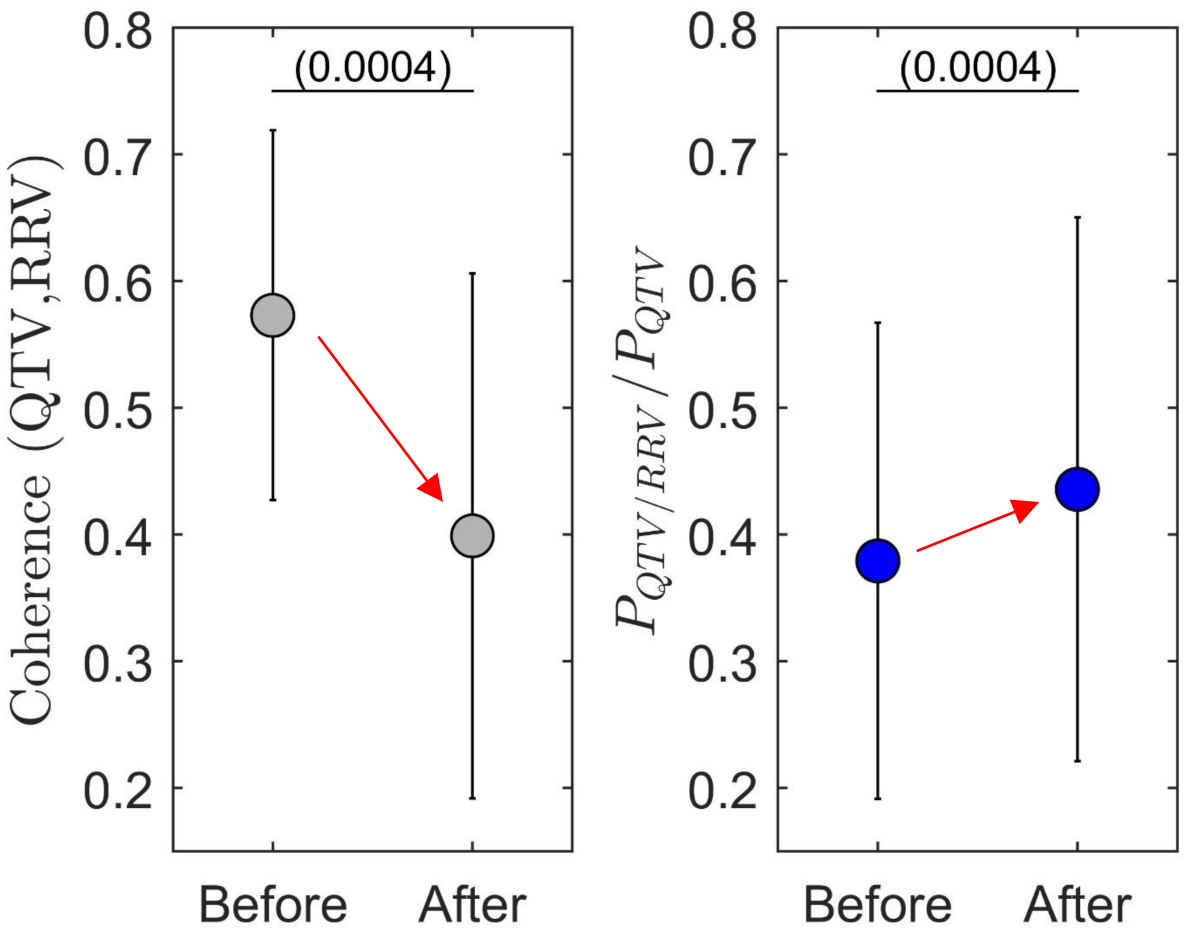
RRV-Unrelated QT Variability

Tilt table test : orthostatic stress -> sympathetic activation

17 healthy subjects Age: 28.2±2.7
- ECG: 1000 Hz



RRV-Unrelated QT Variability



Summary

- (TF) Coherence estimators biased → Partial spectra biased
- We propose a simple method for correcting coherence bias and to improve TF partial spectra accuracy.
- QTV unrelated to RRV estimated by means of unbiased TF partial spectra was about 20% higher than that estimated without correcting for the bias.
- The proposed methodology improves the accuracy of cardio-respiratory and cardiovascular markers, and can provide a better tracking of changes of QTV unrelated to RRV

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